Patent Docket P1726R1PF

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

Leonard Presta

Serial No.: To Be Assigned

Filed: November 15, 2000

For: POLYPEPTIDE VARIANTS WITH

ALTERED EFFECTOR

FUNCTION

Group Art Unit: To Be Assigned

Examiner: To Be Assigned

CERTIFICATE OF MAILING

Thereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner of Patents, Washington, D.C. 20231 on

November 15, 2000

Unn favelly
Ann Savelli

CERTIFICATE RE: SEQUENCE LISTING

BOX SEQUENCE Assistant Commissioner of Patents Washington, D.C. 20231

Sir:

I hereby state that the Sequence Listing submitted herewith is submitted in paper copy and a computer-readable diskette, and that the information recorded in computer readable form is identical to the written sequence listing. I further state that this submission includes no new matter.

Respectfully submitted,

GENENTECH/INC.

Date: November 15, 2000

By: Wendy M. Lee

Reg. No. 40,378

1 DNA Way

So. San Francisco, CA 94080-4990

Phone: (650) 225-1994 Fax: (650) 952-9881

Sequence Listing

- <110> Leonard Presta
- <1205 Polypeptide Variants with Altered Effector Function
- -170 F1720F1F1
- <141> 2000-11-15
- ≈150> US 09/483,588
- <151 > 2000-01-14
- <150> US 60/116,020
- < 51> 1999-01-15
- <160> 11
- <...100 1
- <.:130 218
- <.:1: PF:T
- <:110 Artificial Sequence</pre>
- <.1200
- Sequence is completely synthesized
- <.;()(0) 1
- Asp. The Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val $\frac{1}{5}$
- Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Lys Pro Val Asp
- Gly Glu Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly ± 6
- bys Ala Pro Lys Lou Let Ile Tyr Ala Ala Ser Tyr Leu Glu Ser
- Gly Val. Pro Ser Ang Phe Ser Gly Ser Gly Ser Gly Thr Asp. Pho 75
- Thr Leu Thr Ile Ser Ser Leu Glr. Pro Glu Asp Phe Ala Thr Tyr 80
- Tyr Cys Gln Gln Ser His Glu Asp Pro Tyr Thr Phe Gly Gln Gly
- Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe 110 115 126
- The Phe Pro Pro Ser Asp Glu Glr. Leu Lys Ser Gly Thr Ala Ser 1.15 150 150
- Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val 140 145 150

Gin Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gli Giu 165

Ser Val Thr Giu Gin Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser 175

Lea Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val 185

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Fro Val Thr 200

Lys Ser Phe Ash Arg G'y Glu Cys 215

<210> 2

<:11> 451

<: 12> PRT

<.13> Artificial Sequence

<. 2765

<.i.b> Sequence is completely synthesized

<400>-2

Gun Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly 1 5 10 1!

Gly Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Tyr Ser lle Thr 0

Ger Gly Tyr Ser Trp Asn Trp Ile Arg Gir Ala Pro Gly Lys Gly 40

beu Glu Trp Val Ala Ser Ile Lys Tyr Ser Gly Glu Thr Lys Tyr $^{6.0}_{-0.0}$

Asn Pro Ser Val Lys Gly Arg Ile Thr Ile Ser Arg Asp Asp Ser $\frac{3}{75}$

Lys Asn Thr Phe Tyr Leu Gl
n Met Asn Ser Leu Arg Ala Glu Asp ± 0

This Ala Val Tyr Tyr Cys Ala Arg Gly Sor His Tyr Phe Gly His $\frac{10\%}{10\%}$

Trp His Phe Ala Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser 110 115

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Sen 1.5

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val 140 146 160

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly 165 160 165

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gli Ser 175 Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser per healthy the Gla thr Tyr lie Cys Ash Val Ash His Lys In-Ser Ash The Lye Val Asp Lys Lye Val Glu Pro Lys Ser Cys Asp Lys Thr Eis Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu 250 114.5 Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Ach Trp Tyr Val Asp Gly 285 Val Glu Val His Ast. Ala Lys Thr Lys Fro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Ang Val Val Ser Val Let Thr Val Leu His Glt. --1) 315 3() h Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Cly Gln Pro Arg Glu Pro Gln Val Tyr Thr Lot Pro Pro Ser Arg Glu $[\hat{\beta}^{(0)},(1)]$ Glu Met Thr Lys Ash Gln Val Ser Leu Thr Cys Leu Val Lys Gly $\beta \in \mathbb{N}$ Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Ash Gly Gir. 385 380 Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp 364, ...(10) Gly Ser Phe Phe Let Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asi. Val Phe Ser Cys Ser Val Met His Glu Al.: 4.30 Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly 445440

Lys

400 Pro 1	Ala Ala	Pro	Gla	heu 5	Leu	Gly	Gly	Pro	Ser 10	Val	The	Tu Call	I.}1€2	Pro-
Fre	Lys	Pro	Lys	Asp 20	Thi	heu	Met	110	Ser 25	Итq	Thr	Pro	Glu	Val
Chr	Сув	Val	Val	Val 25	Asp	Val	Ser	His	G1u 40	Asp	Pro	Glu	Val	Lys 45
Phe	Asn	Trp	Tyr	Val 50	Asp	GlΣ	Val	Glu	Val 55	His	Asn	Ala	Lys	Thr 60
Lys	Pro	Arg	Glu	Glu 65	Gln	űλ:	Asn	Ser	Thr 70	Tyr	Arg	Vаl	Val	Ser 5
Val	Leu	Thr	Val	heu ¢0	His	Gli.	Asp	Trp	Leu 35	Asn	Gly	Lys	Glu	Tyr
Lys	Cys	Lys	Val	Ser 35	Asn	Lys	Ala	Leu	Pro 100	Ala	Pro	Tle	Glu	Lys 105
Thr	Ile	Ser	Lys	Ala 110	Lys	Gly	Gln	Pro	Arg 115	Glu	Pro	Gln	Val	T;r
Thr	Leu	Pro	Prc	Ser 125	Arg	Glu	Glu	Met	Thr 130	Lys	Asr.	Gln	Val	Ser 1 · S
Leu	Thr	Cys	Leu	V 41 140	Lys	Gly	Phe	Tyr	Pro 145	Ser	Asp	Ile	Ala	Val 150
Glu	Tip	Glu	Ser	Asr. 155	Gly	Glı.	Pro	Glu	Asn 160	Asn	Tyr	Lys	Thr	That 165
Pro	Pro	Val	Leu	Asp 170	Ser	Asj,	Gly	Ser	Phe 175	Phe	Leu	Tyr	Ser	Lys 150
Leu	Thr	Val	A.sp	ьуs 135	Ser	Arq	Trp	Gln	Gln 190	Gly	Asn	Val	Phe	Sen 1 45
Cys	Ser	Val	Met	His 200	Glu	Ala	Leu	His	Asr. 205	His	Tyr	Thr	Gln	Lys 21(
Ser	Leu	Ser	Leu	Ser 215	Pro	Gly	Lys							

<400> 4

Pro Ala Pro Glu Leu Leu Gly Gly Fro Ser Val The Leu The Pro 1 () Pro Lys Fre Lys Asp Thr Leu Met lie Ser Arg Thr Fre Glu Val The Cyr Val Val Val Asp Val for His Gir Asp Dr. Gin Val Lys The Asm Tr: Tyr Va. Asp Gly Val Glu Val His Ash Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Glr. Asp Trp Leu Ash Gly Lys Glu Tyr 8.5 Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys 55 Thr The Ser Lys Ala Lys Gly Gln Pro Ard Glu Pro Gln Val Tyr 110 Thr Leu Pro Pro Ser Arg Asp Glu Leu Th: Lys Asm Glm Val Ser 130 Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp lle Ala Val 1412.40 Glu Trp Glu Ser Asr. Gly Glr. Pro Glu Asr. Asn Tyr Lys Thr Thr 165 Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln G... Gly Asn Val Phe Ser 1.85 Cys Ser Val Met His Glu Ala Leu His Ash His Tyr Thr Gln Lys 200

Ser Leu Ser Leu Ser Pro Gly Lys 215

-00100 - 5

 $\cdot 10111 \cdot 217$

-1.1121- PET

+1.1130 homo sapiens

 $-(400) \cdot 5$

Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro 1 5 15

Lys Pro Lys Asp Thr Leu Met Ile Ser Ang Thr Pro Glu Val Thr 20 30

Cys Val Val Val Asp Val Ser His Glu Asp Fro Glu Val Gln Phe Ash Trp Tyr Val Rep Gly Val Glu Val H.s Ash Ala Lys The Lys In a Arg Shu Glu Gu. The Arm for The The Arg Vel Vel for Vol Lou The Val Val Els Glm Asp Trp Lou Ash Gly Lys Glu Tyr Lys Cys Lys Val Ser Ann Lys Gly Leu Pre Ala Pro Ile Glu Lys Tir The Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gin Val Tyr Thr 1:0 Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu 1.:5 Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp lle Ala Val Glu 143 Trp Glu Ser Ash Gly Gln Pro Glu Ash Acr. Tyr Lys Thr Thr Pro -155 -160Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gay Asn Val Phe Ser Cys Ser Val Met His Gra Ala Leu His Asn His Tyr Thr Gln Lys Ser (0.00)Let Ser Let Ser Pro Gly Lys 2.1 +0.7100 + 6...11: ...18 -1.112 PRT 1.13 homo sapiens -1400.- 6

Lys Pro Ard Glu Glu Glm Phe Ash Ser Thr Phe Ard Val Val Ser 65 Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Ty: Typ Cys bys Mal Per Arm Typ Ala ben Pro Ala bre The Chu Lys 100 Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Fro Gln Val Tyr 115 Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Vai Ser Leu Thr Cys Leu Val Lys Gly Fhe Tyr Pro Ser Asp Ile Ala Val 145 Glu Trp Glu Ser Ser Gly Gln Pro Glu Asn Asn Tyr Asn Thr Thr 1 € 0 Pro Pro Met Leu Asp Ser Asp Gly Ser Pre Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Ile Phe Ser Cys Ser Val Met H.s Glu Ala Leu His Asn Arg Phe Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys ::1E

+0.0100 + 7 +0.0110 + 218

-1.1121- PRT

Hull3: homo sapiens

 $+(400) \times 7$

Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro 1 5 10

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val ± 6 ± 6 ± 6

Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln 35 40 45

Phe Asr Trp Tyr Val Asp Gly Val Glu Val His Asr Ala Lys Thr -60

Lys Pro Arg Glu Glu Glr Phe Asn Ser Thr Tyr Arg Val Val Ser 65

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr 80 85 90

Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser He Glu Lys 100 Thr lie Ser Lys Ala Lys Giy Gl: Pro Arg Glu Pro Gln Val Tyr 115 The few Pro Pro Ser Clim Clum Glum Met The Lys Ash Clim Mad Cer 130 Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp 11e Ala Val Glu Trp G.x Ser Ann Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu A:p Ser Asp Gly Ser The Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser 1:.0 Cys Ser Val Met His Glu Ala Leu His A:n His Tyr Thr Gln Lys 2+0 205 Ser Leu Ser Leu Ser Leu Gly Lys

215

<31.0% &

KR11: R15

HILL PRT

HALE Mus musculus

-140 oc - 8

Thr Val Prc Glu Val Ser Ser Val Phe Ile Phe Pro Pro Lys Pro 1

Lys Asp Val Leu Thr Ile Thr Leu Thr Pro Lys Val Thr Cys Val

Val Val Asp Ile Ser Lys Asp Asp Pro Glu Val Gln Phe Ser Trp 3 €

Phe Val Asp Asp Val Glu Val His Thr Ala Gln Thr Gln Pro Arg

Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser Val Ser Glu Leu Pro ÖC

The Met His Glr. Aup Cys Leu Asn Gly Lys Glu Phe Lys Cys Arg z(0)

Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr Ile Ser 105 100

Lys Thr Lys Gly Ard Pro Lys Ala Pro Gln Val Tyr Thr Ile Pro 110

Fro Fro Lys Giu Glin Met Ala Lys Asp Lys Val Ser Leu Thr Cys 135.

Met Ile Thr Asp Fhe Fine Fro Glu Asp Lee Thr Val Giu Trp Glin 110.

Trp Asi Gly Glin In. Ala Giu Asi Tyr Lys Asi Thr Glin In 110.

Met Asp Thr Asp Gly Ser Tyr Fhe Val Tvr Ser Lys Leu Asi Val 180.

Glin Lys Ser Asi Trp Glu Ala Gly Asi Thr Phe Thr Cys Ser Val 195.

Leu His Glu Gly Leu His Asi His His Thr Glu Lys Ser Leu Ser 210.

His Ser Pro Gly Lys

<210> "

<211> 118

<212> ERT

<213> Mus musculus

<400> "

Pro Ala Pro Ash Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro 1 5 10 15

Pro Lys Ile Lys Asp Val Leu Met Ile Ser Leu Ser Pro Ile Val 10 $^{\circ}$

Thr Cys Val Val Val Asp Val Ser Glu Asp Asp Pro Asp Val Glu 40

The Ser Trp Phe Val Asn Asn Val Glu Val His Thr Ala Gln Thr $_{10}$

Glr. Thr His Arg Glu Asp Tyr Asn Ser Thr Leu Arg Val Val Ser $\frac{1}{75}$

Ala Leu Pro Ile Gl
n His Gl
n Asp Tr
p Met Ser Gly Lys Glu Phe ± 0

Lys Cys Lys Val Ash Ash Lys Asp Leu Pro Ala Pro Ile Glu Arg -95 -100 -100

Thr The Ser Lys Pro Lys Gly Ser Val Arg Ala Pro Gln Val Tyr 110 11f 1.0

Val Lou Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln Val Thr 1.35 150 156

Leu Thr Cys Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr Val 140 145 150

Glu Trp Thr Asn Ash Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr 165

Glu Fro Val Leu Asp Ger Asp Gly Ser Tyr Phe Met Tyr Ser Lys 100

Leu Arg Val Glu Lyr Lys Ash Trp Val Glu Ard Ash Ser Tyr Ser Lys 195

Cys Ser Val Val His Glu Gly Leu dis Ash Ris His Thr Thr Lys 200

Ser Phe Ser Arg Ter Pro Gly Lys 215

<210> 10 <211> 218

<212> PRT

<213> Mus musculus

<400> 10

Pro A.a Pro Ash Leu Glu Gly Gly Pro Ser Val Pho Ilo Phe Pro 1 10 10 10 25

Pro Ast Ile Lys Asp Val Leu Met Ile Ser Leu Thr Pro Lys Val

Thr Cys Val Val Val Asp Val Ser Glu Asp Asp Pro Asp Val G.n ± 6

Ile Sor Trp Phe Val Asr. Asr Val Glu Val His Thr Ala Gln Ti.r $65\,$

Gln Tilr His Arg Glu Asp Tyr Asn Ser Tilr Ile Arg Val Val Ser 0.5

His Lew Pro Ile Glr. His Gln Asp Trp Met Ser Gly Lys Glu Phe ± 6 - $\times 6$

Lys Cys Lys Val Asn Asn Lys Asp Leu Pro Ser Pro Ile Glu Arg 96 100 100

Thr Ile Ser Lys Pro Lys Gly Leu Val Ang Ala Pro Gln Val Tyr 110 \$110 110

Thr Leu Pro Pro Pro Ala Glu Gln Leu Sor Arg Lys Asp Val Sor 185 180 180

Leu Thr Cys Leu Val Val Gly Phe Asn Pho Gly Asp Ile Ser Val

Glu Trp Thr Ser Asr. Gly His Thr Glu Glu Asr Tyr Lys Asp Thr 155 165

Ala Pro Val Leu Asp Ser Asp Gly Ser Tyr Phe lle Tyr Ser Lys 170 170 175



Leu Ash Met Lys Thr Ser bys Trp Glu bys Thr Asp Ser Fhe Ser 185 195

Cys Ash Val Arg Eis Glu Gly Leu Lys Ash Tyr Tyr Leu Lys Lys 200 200 200

The He Ber Ard for Pro Cly lys 215

<210> 11

5211 - 218

- 212 - ERT

<213> Mus musculus

<400> 11

Fro Pro Gly Asn I'e Leu Gly Gly Pro Ser Val Phe Ile Phe Pro 1 5 1)

Pro Lys Pro Lys A.p Ala Leu Met Ile Ser Leu Thr Pro Lys Val

Thr Cys Val Val Val Asp Val Ser Glu Asp Asp Pro Asp Val His

Val Ser Trp Phe Val Asp Asn Lys Glu Val His Thr Ala Trp Thr

Gln Pro Arg Glu Ala Gln Tyr Asn Ser Tar Phe Arg Val Val Ser

Ala Leu Pro Ile Gli His Glin Asp Trp Mat Arg Gly Lys Glu Proton \mathbb{R}^n

Lys Cys Lys Val Ash Ash Lys Ala Leu Pro Ala Pro Ile Glu Ash $\frac{95}{100}$

Thr Ile Ser Lys Pro Lys Gly Arg Ala Gln Thr Pro Gln Val Tyr 110 115 1.0

Thr Ile Fro Pro Pro Arg Glu Glu Met Ser Lys Lys Lys Val Ser 135

Leu Thr Cys Leu Val Thr Asn Phe Phe Ser Glu Ala Ile Ser Val 140 140 140

Glu Trp Glu Arg Ash Gly Glu Leu Glu Gin Asp Tyr Lys Ash Thr 155 166 166

Pro Pro Ile Leu Asp Ser Asp Gly Thr Tyr Phe Leu Tyr Ser Lys 170 175 180

Leu Thr Val Asp Thr Asp Ser Trp Leu Glr. Gly Glu Ile Phe Thr 185 196 196

Cys Ser Val Val Hir Glu Ala Leu His Ash His His Thr Gln Lys 200-205-205

